In re Application of:

Worley and Brakeman Application No.: 09/910,706

Filed: July 20, 2001

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PATENT Attorney Docket No.: JHU1520-2

AMENDMENTS

A. <u>IN THE CLAIMS</u>:

Please enter the following rewritten claims:

10. (Currently Amended) A method of selecting a compound that interferes with binding of a synaptic activation protein to a cellular binding protein in the mammalian central nervous system, comprising:

adding a test compound to a reaction mixture containing (i) a synaptic activation protein having at least 70% sequence identity to a polypeptide having the sequence SEQ ID NO:2, (ii) a binding protein to which the synaptic activation protein binds, and (iii) means for detecting binding between the synaptic activation protein and the binding protein; measuring binding between the synaptic activation protein and the binding protein; and

selecting the compound if the measured binding is greater than or less than binding measured in the absence of the test compound.

- 11. (Currently Amended) The method of claim 10, wherein the binding protein is a metabotropic glutamate receptor (mGluR).
- 12. (Currently Amended) The method of claim 27, wherein the binding protein comprises a mGluR and the measuring the cellular response to binding between the synaptic binding protein and the binding protein comprises measuring phosphoinositidase C (PI-PLC) activity in the cells.

Please enter the following new claims:

--13. (New) The method of claim 10, wherein the binding protein is a metabotropic glutamate receptor comprising a sequence selected from the group consisting of SSSL and SSTL.

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- 14. (New) The method of claim 11, wherein the mGluR is selected from mGluR5 and mGluR1α.
- 15. (New) The method of claim 10, wherein the synaptic activation protein is a Homer protein.
- 16. (New) The method of claim 10, wherein the synaptic activation protein is in solid phase.
 - 17. (New) The method of claim 16, wherein the solid phase is a microtiter plate.
- 18. (New) The method of claim 10, wherein the means for detecting binding is a glutathione-S-transferase (GST)-pulldown.
- 19. (New) The method of claim 10, wherein the means for detecting binding is coimmunoprecipitation.
- 20. (New) The method of claim 10, wherein the measuring binding comprises labeling the binding protein, wherein the labeling is direct labeling or is subsequent addition of a labeled, binding protein-specific reagent.
- 21. (New) The method of claim 20, wherein the binding protein-specific reagent is an antibody.
- 22. (New) The method of claim 20, wherein the labeling comprises use of an enzyme capable of generating a signal, use of a radiolabeled reagent, use of a fluorescent dye, or use of gold or biotin.
- 23. (New) The method of claim 22, wherein the radiolabeled reagent is labeled with 125I.

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- 24. (New) A pharmaceutical composition containing a compound identified by the method of claim 10.
- 25. (New) A method of treating a condition comprising administration of an effective amount of a compound identified by the method of claim 10, wherein the condition is characterized by an altered neuronal and/or synaptic activity.
- 26. (New) The method of claim 25, wherein the condition comprises epilepsy, abnormal brain development, neural injury, trauma or chemical addiction.
- 27. (New) A method of identifying a compound that modulates a cellular response, comprising:

adding a test compound to a cell containing: (i) a synaptic activation protein having at least 70% sequence identity to a polypeptide having the sequence SEQ ID NO:2, (ii) a binding protein to which the synaptic activation protein binds, and (iii) means for detecting cellular response to binding between the synaptic activation protein and the binding protein;

measuring the cellular response to binding between the synaptic activation protein and the binding protein; and

comparing the cellular response in the presence and absence of the test compound, wherein a change in the cellular expression in the presence of the compound as compared to the absence of the compound is indicative of a compound that modulates a cellular response.

- 28. (New) The method of claim 27, wherein the cell comprises a bacterial, yeast, insect or mammalian cell.
- 29. (New) The method of claim 27, wherein the synaptic activation protein is expressed by a gene endogenous to the cell.

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- 30. (New) The method of claim 27, wherein the synaptic activation protein is expressed by a gene construct transfected into the cell.
- 31. (New) The method of claim 27, wherein the binding protein is expressed by a gene endogenous to the cell.
- 32. (New) The method of claim 27, wherein the binding protein is expressed by a gene construct transfected into the cell.
- 33. (New) The method of claim 27, wherein the measuring the cellular response to binding between the proteins comprises a two-hybrid protein interaction assay.
- 34. (New) The method of claim 27, wherein the measuring the cellular response to binding between the proteins comprises using a reporter construct.
- 35. (New) The method of claim 34, wherein the reporter construct comprises a vector comprising a polynucleotide encoding an isolated synaptic activation protein having at least 70% sequence identity to a polypeptide having the sequence SEQ ID NO:2.
- 36. (New) The method of claim 35, wherein the reporter construct further comprises at least one regulatory sequence.
- 37. (New) The method of claim 27, wherein the measuring the cellular response to binding between the proteins comprises using a mGluR construct comprising a binding protein, wherein the binding protein comprises mGluR.
- 38. (New) The method of claim 37, wherein the mGluR comprises a sequence selected from the group consisting of SSSL and SSTL.
- 39. (New) The method of claim 37, wherein the mGluR is selected from mGluR5 and mGluR1α.

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- 40. (New) The method of claim 27, wherein the cellular response comprises an increase or decrease in calcium mobilization or PI-PLC activity.
- 41. (New) A pharmaceutical composition containing a compound identified by the method of claim 27.
- 42. (New) A method of treating a condition comprising administration of an effective amount of a compound identified by the method of claim 27, wherein the condition is characterized by an altered neuronal and/or synaptic activity.
- 43. (New) The method of claim 42, wherein the condition comprises epilepsy, abnormal brain development, neural injury, trauma or chemical addiction. --